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Effects of Immobilization with Medetomidine and Reversal with Atipamezole on Blood Chemistry of Semi-Domesticated Reindeer (*Rangifer tarandus tarandus* L.) in Autumn and Late Winter

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Departments of [1]Basic Veterinary Sciences and [2]Clinical Veterinary Sciences, Faculty of Veterinary Medicine, University of Helsinki, and [3]Orion Corporation, Turku, and [4]Game and Fisheries Research Institute, Reindeer Research, Kaamanen, Finland.

Soveri T, Sankari S, Salonen JS, Nieminen M: Effects of immobilization with medetomidine and reversal with atipamezole on blood chemistry of semi-domesticated reindeer (*Rangifer tarandus tarandus* L.) in autumn and late winter. Acta vet. scand. 1999, 40, 335-349. – Blood chemistry was studied in 8 adult female reindeer, of which 5 were pregnant. Half of them received only medetomidine (150 μg/kg i.m.) and half of them medetomidine and atipamezole (750 μg/kg) in March. Three weeks later the drug regimens were reversed. The same procedure was carried out during the next September and October. Seasonal differences in pretreatment values could be seen in serum urea, phosphorous, and cholesterol, with the highest concentrations during the autumn; and creatinine, ASAT, ALAT, and CK values, which were higher in the non-pregnant reindeer in late winter. Their low-protein and low-energy diet during the winter explains most of the differences. Increased enzyme activities in serum indicate decreased membrane stability of certain organs in late winter, possibly due to nutritional deficiencies. Treatment effects could be seen in several parameters. The increase in blood glucose and decrease in serum FFA were most probably due to α_2-adrenoceptor activation, which inhibits insulin release and lipolysis. These effects were partly or totally inhibited after treatment with the antagonist atipamezole. The earlier increase in serum CK and ASAT activities in those receiving atipamezole can be explained by increased tissue perfusion due to atipamezole itself and the fact that these animals stood up and began to move much earlier than did those which received medetomidine only. A significant decrease in serum Na^+, K^+, Cl^-, Pi, cholesterol, total Ca, and total protein concentration observed during the first 10 to 40 min of the medetomidine sedation could be explained by possible haemodilution and diuresis. More effective metabolism of medetomidine in autumn could explain the shorter recovery times of reindeer receiving only medetomidine and most of the differences in treatment effects between the seasons: faster increase in protein and cholesterol concentrations after the decrease, and the antagonistic effect of atipamezole on glucose and Pi changes in autumn. Based on these results, medetomidine seems to be a good sedation agent for reindeer both in autumn and in late winter; the effects of medetomidine can be rather effectively antagonized by atipamezole.

seasonality; resedation; pregnancy.

Introduction

Medetomidine, a relatively new potent α_2-adrenoceptor agonist, has been widely used alone or particularly in combinations with other agents for immobilization in domestic and nondomestic animals including many ruminant species (*Jalanka* 1988, *Jalanka & Roeken* 1990, *Jalanka* 1993, *Arnemo et al.* 1994, *Arnemo* 1995). Atipamezole has been successfully used as a reversal agent, which increases markedly medetomidine's value as a practical immobilizing agent in zoo- and wildlife medicine.

Medetomidine alone induced complete immobilization of semi-domesticated Norwegian reindeer (*Rangifer tarandus tarandus* L.), (*Tyler et al.* 1990, *Ranheim et al.* 1997), but was insufficient to immobilize Svalbard reindeer (*Rangifer tarandus platyrhynchus), (Tyler et al.* 1990). The environmental physical conditions and diet of the reindeer change significantly during the year. The semi-domesticated reindeer eats green vegetation during the brief summer season (*Nieminen & Heiskari* 1989). During the winter reindeer mainly dig under the snow for lichens (*Nieminen & Heiskari* 1989), which contain mainly soluble carbohydrates and are poor in proteins, fats, minerals, and vitamins (*Pulliainen* 1971, *Nieminen & Heiskari* 1989). These winter conditions are reflected in their rumen ciliate fauna (*Westerling* 1970), papillar morphology in the reindeer rumen (*Soveri & Nieminen* 1995), blood characteristics (*Hyvärinen et al.* 1975 & 1977, *Nieminen* 1980, *Soveri et al.* 1992), and liver histology (*Soveri* 1993). Biotransformation in the liver is the most important route of medetomidine elimination (*Salonen & Eloranta* 1990, *Salonen* 1991). Thus, changes in the size and histology of the reindeer liver (*Bjarghov* 1977, *Soveri* 1993), as well as reduced metabolic rate (*Nilssen et al.* 1984) during the winter season, may have an effect on the metabolism of medetomidine. Marked seasonal differences in effective doses of another α_2-agonist, xylazine, were found in the moose (*Alces alces), (Garner & Addison* 1994), but in reindeer *Ranheim et al.* (1997) found no seasonal variation in drug disposition based on the pharmacokinetic parameters of medetomidine or atipamezole. Atipamezole alone may also have some direct or indirect effects on their physiology and blood chemistry. The purpose of this study was to investigate the effects of medetomidine and atipamezole on the blood chemistry of reindeer, and the effects of season and pregnancy on these responses.

Materials and methods

Animals

The investigation was carried out at the experimental station of the Reindeer Herding Association at Kaamanen, Finnish Lapland (latitude 69° 10′ N). The 8 semi-domesticated reindeer were allowed to graze freely under natural conditions. A few days before the experiment they were herded into pens and fed with lichens. No food was given during the days when the experiments were carried out.

The 8 adult females, aged 1.5 to 11.5 years, weighing 69 to 88 kg, 5 pregnant in late winter, were randomly assigned to 2 groups in March 1991 so that 4 of them received in the first period only medetomidine (medetomidine hydrochlorid 10 mg/ml, Orion Corp. Animal Health Division, Turku, Finland) 150 μg/kg in the left triceps muscle. After a three-week washout period, they received medetomidine and atipamezole (Antisedan® 5 mg/ml, Orion Corp. Animal Health Division, Turku, Finland). Atipamezole was given 750 μg/kg in the right triceps muscle 30 min after the medetomidine. The remaining 4 of the 8 animals were treated in reverse order. The same procedure was repeated in September and October 1991, four of the reindeer being the same as in the previous experiment. The ages of this group were 2 to 10 years and

weights 71 to 89 kg. The experiments were carried out indoors, where the ambient temperature varied between 10 and 17°C.

The time from medetomidine injection to immobilization in sternal or lateral recumbency was recorded as induction time, and the time from medetomidine or atipamezole injection to rising to a standing position was recorded as on-feet time.

Blood samples

Blood samples were drawn from the jugular vein just before the medetomidine injection and after 0.5, 1, 2, 3, and 5 h into evacuated heparinized tubes for blood glucose determination, and into plaintubes before the injection and after 10, 20, 40, and 50 min and 2, 3, 5, and 8 h for serum chemistry. Serum was separated, frozen in portions and stored at -20°C until analysed.

Blood analysis

Blood glucose was analysed within 2 h with Hypocount MX R® (Hypoguard Ltd., Woodbridge, Suffolk, United Kingdom).

Spectrophotometric methods were used for the determination of total protein (*Weichselbaum* 1946), urea (*Gutmann & Bergmeyer* 1974), creatinine (*Fabiny & Ertigshausen* 1971), inorganic phosphorus (Pi; *Daly & Ertigshausen* 1972), cholesterol (*Allain et al.* 1974), and non-esterified fatty acids (FFA; *Shimizu et al.* 1980) concentrations in serum. The spectrophotometric analyses were performed with an automatic chemistry analyser (KONE Spesific, KONE Instruments Corp., Espoo, Finland).

Serum total calcium (Ca) concentration was analysed by atomic absorption spectrophotometry (Model 2380, Perkin-Elmer Corp., Norwalk, USA).

Serum sodium (Na^+), potassium (K^+), and chloride (Cl^-) concentrations were measured directly by ion-selective electrodes (KONE Micrrolyte 2+3, KONE Instruments Corp., Espoo, Finland).

The serum activities of alkaline phosphatase (AP), creatine kinase (CK), aspartate aminotransferase (ASAT), and alanine aminotransferase (ALAT) were determined according to the recommendations of the SCE (*Scandinavian Society for Clinical Chemistry and Clinical Physiology* 1974, 1979).

Statistical analyses

Carry-over and period effects were tested by t-test procedures as described by *Jones & Kenward* (1989). These tests were run separately for both seasons and for all time-points.

In cases of nonsignificant carry-over effects, the data from both periods and both seasons were used to study treatment effects, seasonal variation, temporal patterns, and effects of pregnancy by repeated measures analyses of variance with season and pregnancy as between-factors and treatment and time after injection as within-factors. Significance of time-factor and corresponding interactions were evaluated by means of Greenhouse-Geisser adjusted p-values. Differences in changes between successive time-points as well as in changes from baseline were also tested. In addition seasonal differences and effects of pregnancy in pretreatment values were subjected to t-tests. Significance was declared at $p < 0.05$.

Results

No carry-over effects could be seen in any of the parameters.

The seasonal effects on pretreatment values are given in Table 1. Seasonal differences in pretreatment values in all animals could be seen in the following variables: urea and Pi concentrations were higher during the autumn, and creatinine was at a higher level during the late winter. The seasonal change in urea values could be seen also as a period effect between the 2 ex-

Table 1. Serum and blood constituents of female reindeer in September and in April. Mean (± SE).

Variable	April, pregnant 1991 (n=5)	April, non-pregnant 1991 (n=3)	September 1991 (n=8)
Total protein (g/l)	64.8[a] (3.95)	85.8[b] (1.27)	82.9 (2.72)
Urea (mmol/l)	5.3[a] (1.60)	9.1[a] (0.10)	15.0 (1.38)
Creatinine (mmol/l)	210[a] (17.7)	160[a] (15.2)	123 (15.2)
Cholesterol (mmol/l)	1.9 (0.25)	1.2[a] (0.18)	2.1 (0.09)
Free fatty acid (mmol/l)	1.1 (0.34)	0.7 (0.12)	1.2 (0.17)
Glucose (mmol/l)	3.2 (0.20)	3.6 (0.14)	3.5 (0.30)
Na^+ (mmol/l)	151 (1.2)	151 (0.9)	149 (0.8)
Cl^- (mmol/l)	100 (1.6)	103 (1.5)	99 (1.1)
K^+ (mmol/l)	4.4 (0.25)	4.5 (0.12)	4.4 (0.13)
Ca (mmol/l)	2.3[a] (0.07)	2.6 (0.13)	2.8 (0.07)
Pi (mmol/l)	2.0[a] (0.07)	2.1 (0.57)	2.9 (0.17)
AP (U/l)	80[a] (12.0)	77 (20.2)	239 (43.5)
ALAT (U/l)	26.8 (2.89)	91.7[a,b] (10.53)	26.9 (2.06)
ASAT (U/l)	62.0 (7.13)	117.3[a,b] (22.48)	66.1 (7.08)
CK (U/l)	323 (118.9)	595[a] (38.7)	311 (48.0)

a) Statistically significant ($p<0.05$) difference when compared to autumn.
b) Statistically significant ($p<0.05$) difference when compared to pregnant animals.

periments 3 to 4 weeks apart: later values in autumn and earlier in late winter were lower. Non-pregnant reindeer had higher CK, ASAT, and ALAT activities and lower cholesterol concentrations than they did in the autumn. The pregnant animals had lower protein, Ca, and AP values in late winter in comparison to the autumn values. Protein, ASAT, and ALAT values were lower in the pregnant than in the non-pregnant in late winter.

The treatments had variable effects on most of the analytes measured. Only AP values remained constant during the follow-up period in all reindeer in both seasons. Treatment effects on some of the parameters are shown in Figs. 1-6.

The blood glucose concentration increased during the first 30 min after the medetomidine administration (Fig. 1). After the atipamezole dose, the glucose response curves of the groups differed. Atipamezole clearly stabilized blood glucose in autumn, whereas values in the medetomidine group continuously increased towards the 2-h sample level and remained above the values of the atipamezole group to the end of the observation period. In winter, despite the atipamezole treatment, blood glucose continued increasing slowly towards the end of the experiment, reaching the final level of the medetomidine-treated animals.

Serum protein concentrations first decreased both in autumn and late winter and were at their lowest level in 40-min and 50-min samples; after that they gradually returned to or near the pretreatment level (Fig. 2). Treatment effects could be seen in autumn, when protein concentrations of those which received no atipamezole increased more quickly after the decrease: a clear increase could already be observed in the 2-h sample. In winter pregnant reindeer had a smaller decrease in protein levels within the first hour and a smaller increase afterwards than did the non-pregnant.

Treatments seemed to have little effect on

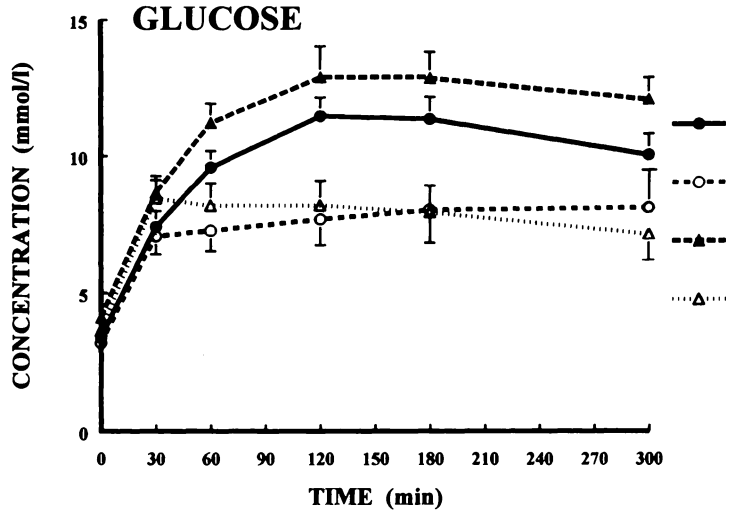

Figure 1. Effects of medetomidine (150 μg, given at 0 min) and atipamezole (750 μg, given at 30 min) on blood glucose concentrations (mean ± SEM) of reindeer. ● = reindeer in late winter which received only medetomidine, ○ = or medetomidine and atipamezole; ▲ = reindeer in autumn which received only medetomidine, △ = or medetomidine and atipamezole.

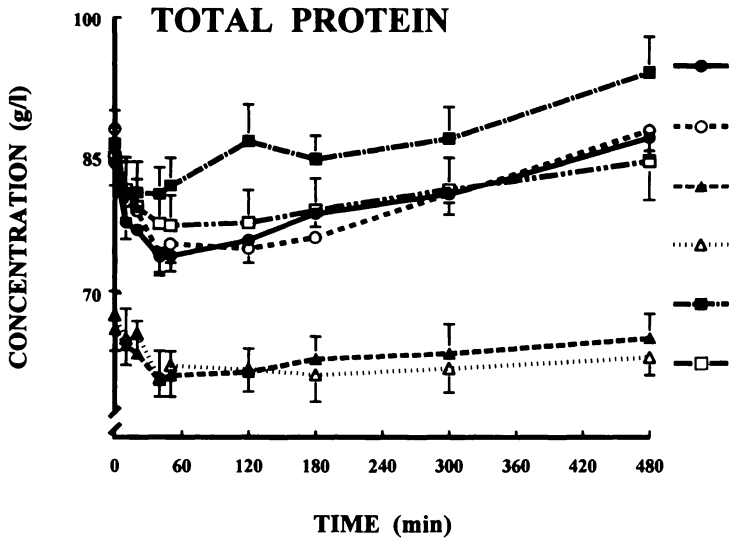

Figure 2. Effects of medetomidine and atipamezole on serum total protein concentrations (mean ± SEM) of reindeer. ● = non-pregnant reindeer in late winter which received only medetomidine, ○ = or medetomidine and atipamezole; ▲ = pregnant reindeer in late winter which received only medetomidine, △ = or medetomidine and atipamezole; ■ = reindeer in autumn which received only medetomidine, □ = or medetomidine and atipamezole.

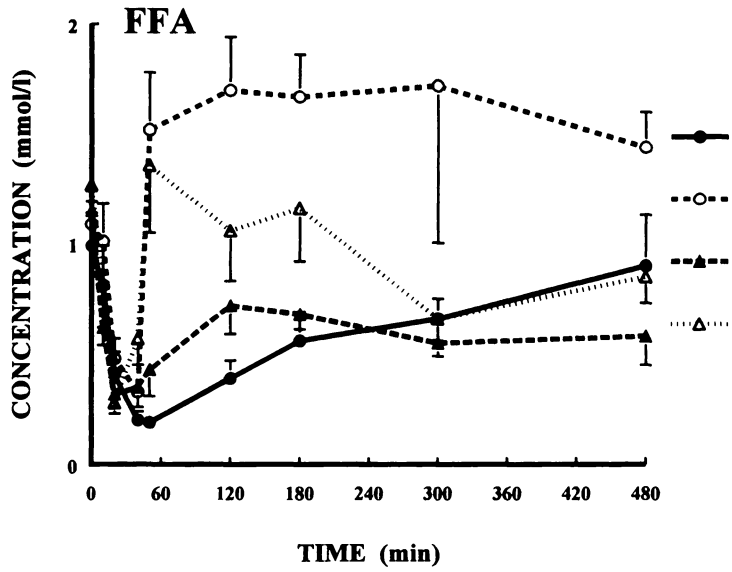

Figure 3. Effects of medetomidine and atipamezole on serum free fatty acid (FFA) concentrations (mean ± SEM) of reindeer. (For abbreviations see Fig. 1.)

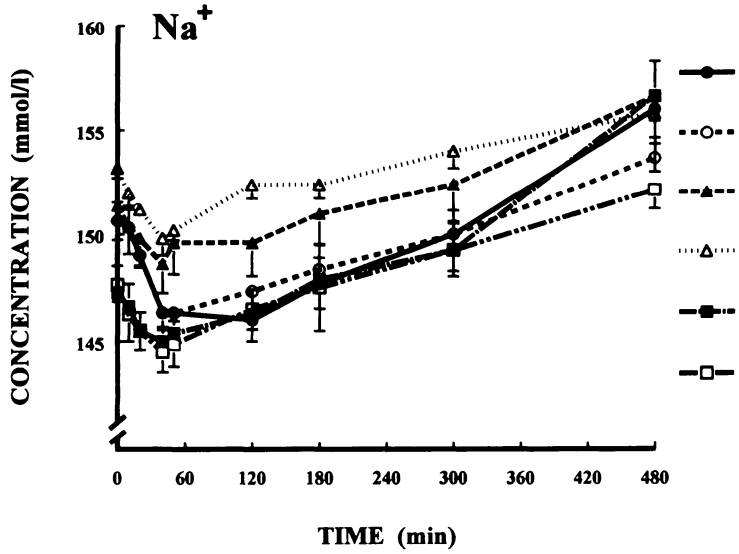

Figure 4. Effects of medetomidine and atipamezole on serum sodium (Na+) concentrations (mean ± SEM) of reindeer.(For abbreviations see Fig. 2.)

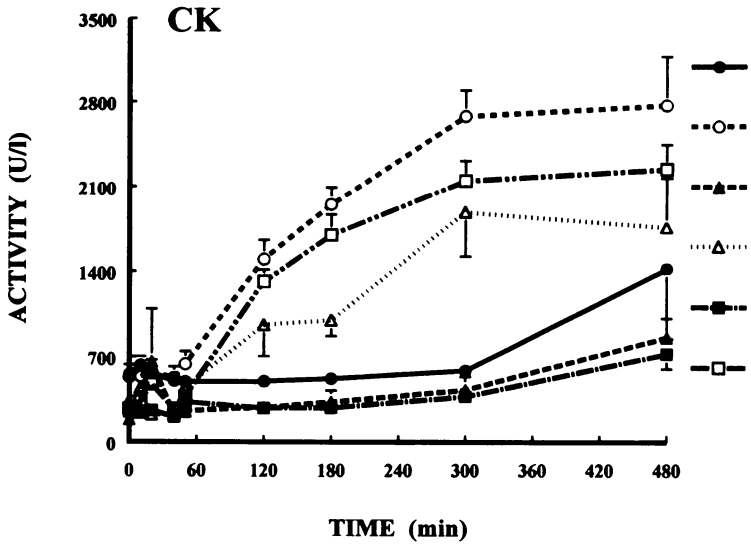

Figure 5. Effects of medetomidine and atipamezole on serum creatine kinase (CK) activities (mean ± SEM) of reindeer. (For abbreviations see Fig. 2.)

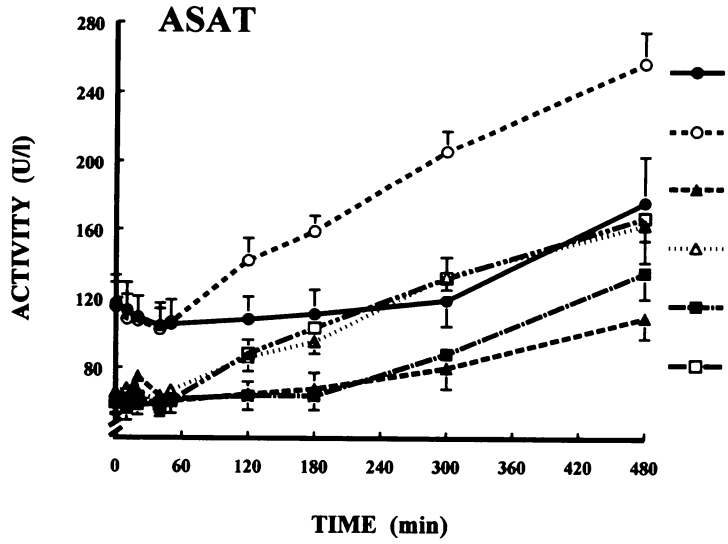

Figure 6. Effects of medetomidine and atipamezole on serum aspartate aminotransferase (ASAT) activities (mean ± SEM) of reindeer. (For abbreviations see Fig. 2.)

serum urea and creatinine concentrations in either season. Urea increased in the last samplings in those which got no atipamezole, and creatinine increased towards the end of the observation period in all of them in both seasons.
The decrease in Ca values 40 min after the medetomidine treatment was more pronounced in autumn. One hour after the medetomidine treatment, Ca values were quite stable in all of the animals except for the autumn medetomidine group, which showed nearly hypocalcemic values for the last 5 h of the experiment.
After medetomidine injection serum Pi decreased in all animals and reached its lowest levels in 20 to 40 min. Then it stayed low, except in animals which received atipamezole in autumn. In those animals, Pi increased soon after atipamezole injection to levels near the first values.
Medetomidine decreased serum cholesterol values in 10 min, and in pregnant animals the values stayed below the pretreatment level for the entire follow-up period. The treatment effect in autumn was the same as was observed for protein.
Serum FFA decreased strongly in the reindeer in the beginning of the experiment, but increased rapidly (in 20 min) after atipamezole injection, to values even over the pretreatment level (Fig. 3). FFA in reindeer which did not receive atipamezole stayed for several hours at low levels and had only a slight tendency to increase towards the end of the observation period.
Medetomidine decreased serum Na^+ (Fig. 4), K^+, and Cl^- concentrations in the beginning of the observation period. Sodium and Cl^- reached their lowest levels in 40 min and K^+ in the first 10 min following the medetomidine dose, after which the values started to normalize. In the last sample, Na^+ and Cl^- concentrations exceeded the values observed before sedation in all animals. In all groups but one this Na^+ concentration was reached already in the 5-h sample. The decrease in K^+ was smaller in the pregnant than in the non-pregnant reindeer in winter.
The time-related responses of the serum electrolyte concentrations differed between the treatments. Serum Na^+ and Cl^- concentrations increased more towards the end of the follow-up period in the medetomidine-treated animals than in animals treated with both medetomidine and atipamezole.
Serum K^+ values stabilized in 1.5 h after the atipamezole treatment at a lower level than in the medetomidine group. After that, the K^+ response to treatment was dependent on season. At the end of the experiment in autumn the serum K^+ concentration of the medetomidine group returned to the level of the atipamezole-treated animals. In winter the K^+ values continued to increase in the medetomidine group until the 3-h sample, and the values remained high to the end of the experiment. In winter also the K^+ values of the atipamezole-treated animals started to increase from the 3-h sample on, and at the end reached the corresponding value of the medetomidine group.
An interaction was observed between treatment and time in the response of serum CK and ASAT activities (Figs. 5 and 6). The difference in these responses between the treatments developed within the first 2 h, when the enzyme activities in the medetomidine- and atipamezole-treated animals were distinctly above baseline and continued to increase during the next 3 h. Responses of the animals which received only medetomidine were much slower, so that they showed increasing values only during the last 3 h of the observation period. In pregnant animals which received atipamezole, CK activities rose more slowly and to lower levels than in corresponding non-pregnant animals in winter. Non-pregnant animals in winter had a small decrease in ASAT activities within the first hour, whereas in pregnant animals the ac-

Table 2. Induction times (min) and on-feet times (min) of reindeer immobilized with medetomidine (M, 150 μg/kg) or immobilized with medetomidine and remobilized after 30 min with atipamezole (M + A, 150 + 750 μg/kg) in autumn (AU) and in late winter (W). N = 8 in all groups.

Treatment, season	Induction time		On-feet time	
	Mean (±SD)	Range	Mean (±SD)	Range
M, AU	3.7 (0.91)	2.3-4.8	345.6[a] (68.89)	210-420
M, W	4.4 (1.12)	3.3-6.8	436.3[a] (37.01)	360-460
M + A, AU	3.5 (0.96)	2.3-5.0	11.0[b] (2.68)	6-15
M + A, W	5.7 (2.85)	3.8-12.5	11.8[b] (2.97)	8-16

a) The time from medetomidine injection to recovery in standing position. Difference between the groups is statistically significant ($p<0.01$).
b) The time from atipamezole injection to recovery in standing position.

tivities did not change during that period.

Serum ALAT activity decreased in all animals after medetomidine injection, being under the pretreatment level for 2 h; then it gradually increased and was higher than the pretreatment value in the last sample. Pregnant animals showed a smaller decrease in the beginning, and a smaller increase in ALAT activities after that than did non-pregnant reindeer in winter.

Induction and reversal times are given in Table 2. The reindeer which received no atipamezole woke up earlier in autumn than in late winter. A resedation was observed within a few hours after reversal in the reindeer which received atipamezole. Those animals showed sternal recumbency and sleepiness, but stood up when approached.

Discussion

Seasonal variation and effect of pregnancy

Decreased serum protein concentrations due to decreased albumin and/or globulin values in winter or because of poor condition have been reported in various cervid species including reindeer (*Franzmann & LeResche* 1978, *Hyvärinen et al.* 1975, *Nieminen* 1980, *Messier et al.* 1987, *Soveri et al.* 1992). Lower total protein concentrations in serum were observed only in pregnant animals in late winter. Considerable increase in blood volume and decrease in serum albumin are documented in pregnant humans (*Greene et al.* 1986).

Low concentrations of proteins and minerals in lichens (*Nieminen & Heiskari* 1989), the natural winter food of the reindeer, may offer most of the explanation for the seasonal variation of serum urea, creatinine, and Pi values in all animals.

Serum concentration of creatinine is a crude estimate of glomerular filtration rate (GFR; *Finco* 1989).The reindeer has limited capacity to concentrate urine (*Valtonen & Eriksson* 1977) and a low-protein diet causes a significant reduction in the GFR and urine osmolality (*Valtonen* 1979). Thus the low protein level in the winter diet may have decreased GFR and increased serum creatinine values. In grazing reindeer, decrease in dietary protein in wintertime is reflected in lower serum urea values in comparison to values in autumn, when the diet contains green vegetation and mushrooms (*Soveri et al.* 1992).

Franzmann & LeResche (1978) found the highest Ca and phosphorous concentrations in the serum of Alaskan moose which were in good condition. *Hyvärinen et al.* (1975) reported low values for Ca, and *Nieminen* (1980) for Ca and phosphorous in reindeer in poor condition dur-

ing the winter. Although our animals were not in poor condition, winter diet and a slight decrease in condition may explain the lower phosphorous values. Lower serum total Ca values in pregnant reindeer are obviously due to lower amounts of albumin-bound Ca.

Decreases in cholesterol values during the winter have been reported in reindeer (*Nieminen* 1980, *Larsen et al.* 1985, *Soveri et al.* 1992) and in other deer species (*Warren et al.* 1981, *Eiben & Fischer* 1984, *Klinger et al.* 1986). This clear seasonal variation may possibly be metabolic in origin, because plants contain no cholesterol.

Low serum AP activities have been found in white-tailed deer fawns and reindeer calves in winter (*Hyvärinen et al.* 1977, *Nieminen* 1980, *Klinger et al.* 1986, *Soveri et al.* 1992), and this has been interpreted as indicating cessation of growth during the winter. The animals in this study were adult, but still the same phenomenon could be observed in pregnant reindeer. The reason for this is unknown.

The increase in serum ALAT activity during the winter agrees well with the observations of *Soveri et al.* (1992) on reindeer calves during the winter and the observations of *Seal et al.* (1978) of white-tailed deer fawns kept on a low-energy diet. This may be a consequence of increased cell membrane permeability in some organs containing ALAT or increase in its overall induction. The higher serum CK and ASAT activities in winter might also suggest leakage from the muscle cells. Nutritional deficiencies may have contributed to the stability of the cell membranes.

Treatment effects

The effect of treatments was studied in relation to peripherial blood. Although some of the effects of medetomidine could be interpreted as α_2-adrenoceptor effects, most effects are, however, most probably secondary and due to a change in haemodynamics (*Ruskoaho & Leppäluoto* 1989, *Vainio & Palmu* 1989). Some effects of atipamezole are clearly reversal to α_2-adrenoceptor agonism, with others being due to earlier recovery of the treated animals. The clearest effects of atipamezole were reflected in glucose, FFA, CK, and ASAT values. Concerning the effects of pregnancy on blood chemistry after the treatments, they were the same: pregnancy decreased the amplitude of the change caused by the treatment. This could be explained by the fact that pregnancy may increase blood volume and thus cause changes in blood chemistry to slow, or metabolic effects of pregnancy as such are responsible for the difference.

The increase in blood glucose after our medetomidine treatment agrees with the finding that activation of α_2-adrenoceptors inhibits insulin release from pancreatic islets (*Nakadate et al.* 1980). A rise in serum glucose has been observed in animals treated with α_2-agonists (*Brockman* 1981, *Gasthuys et al.* 1987, *Jalanka & Roeken* 1990). The antagonistic effect was clearly demonstrated in autumn when atipamezole stopped the increase in blood glucose values and stabilized them. However, the increase in blood glucose could not be totally controlled by atipamezole in winter, possibly due to different medetomidine/atipamezole ratios in the 2 seasons. This could have been a consequence of different metabolisms of these 2 drugs in different seasons. Persistent hyperglycaemia was present in the medetomidine-treated animals for most of the observation period. Reversal with atipamezole could be beneficial in preventing glucose- and water loss in urine; especially when reindeer on a restricted feed supply are sedated.

A significant decrease in serum total protein, total Ca, Pi, cholesterol, Na^+, K^+, Cl^-, and ALAT values was observed during the first 10 to 40 min of the medetomidine sedation, whereas serum urea and creatinine concentra-

tions were quite stable. Medetomidine is known to decrease blood pressure (*Savola* 1989), which together with the recumbent position could increase plasma volume as the interstitial fluids flow into the circulation. Haemodilution is seen in the lowered values of haematocrit, haemoglobin, serum proteins and protein-bound substances like calcium and cholesterol. In the present study, the decrease in the serum total protein, total calcium, and cholesterol concentration is suggestive of haemodilution. Small molecules like urea, creatinine, and electrolytes are unaffected by haemodilution (*Young & Bermes* 1986). The decrease in serum Pi, Na^+, K^+, and Cl^- concentrations at the beginning of the sedation might be caused by medetomidine directly. α_2-adrenoceptor agonists are known to increase diuresis by modulating blood pressure, atrial natriuretic peptide levels, and tubular reabsorption (*Ruskoaho & Leppäluoto* 1989). Increased urine output and decreased urine density has been observed in cattle and horses (*Thurmon et al.*1978, *Gasthuys et al.* 1987). The difference in the time-related response between the treatments in serum urea, Pi, Na^+, and Cl^- values may indicate mild dehydration of the medetomidine-treated animals at the end of the experimental period. The corresponding difference in serum protein concentrations was observed only in autumn.

During the first hour of the experiment, the serum total Ca values were stabilized independent of the treatment in all animals except those which received medetomidine in autumn; their Ca values continued to decrease despite the fact that the corresponding total protein values increased. Without knowledge of the level of ionized Ca it is difficult to evaluate whether the animals with low Ca values were in danger of hypocalcemia.

Serum FFA decreased after medetomidine sedation, apparently because of the inhibitory effect of α_2-adrenoceptor agonists on lipolysis (*McDonald et al.* 1988). Enhanced serum FFA values were observed after the treatment with the antagonist.

Medetomidine caused increases in the serum K^+ concentration during the first 3 h. This time-related response was later dependent on the season. In autumn the K^+ values finally fell below the pretreatment level, as they did also in pregnant reindeer, which got atipamezole in winter, whereas in late winter in other reindeer the values remained above the pretreatment level until the end of the experiment. In winter the K^+ values continued to increase towards the end also in the atipamezole-treated non-pregnant animals. Serum K+ concentrations may indicate changes in acid-base balance. The ruminants are susceptile to impaired ventilation and acid-base disturbances when restrained in a recumbent position.

During sedation the reindeer showed decreased coordination before lying down. Incoordination exposes an animal to muscle traumas, which cause release of muscle enzymes. Lying steadily in one position together with tissue hypoxia during sedation may contribute to this release. The time-related differences in increase of serum CK and ASAT activities between the treatments could be explained by increased tissue perfusion caused by atipamezole (*Salonen et al.* 1995) and by the difference in physical activity of the animals. The reindeer which received atipamezole stood up and walked much earlier than did those which received medetomidine only. Because moving obviously enhanced lymphatic and blood circulation, increased muscle enzyme activities were found earlier in the systemic circulation of mobile animals than in those sedated for a longer time. The follow-up period should have been longer to demonstrate whether the corresponding values in the medetomidine-treated animals would have been higher, indicating more severe or more extensive muscle lesions.

Times to recovery of these reindeer which did not receive atipamezole were shorter in autumn than in winter. Interpretation of this is difficult, because various uncontrolled factors, like noise, may affect recovery times. The more effective metabolism of medetomidine could, however, be the reason for this more rapid recovery. Lower medetomidine concentrations and smaller medetomidine/atipamezole ratios in autumn could also explain most of the differences in treatment effects between the seasons: faster increases in protein and cholesterol concentrations after the decrease, and the antagonistic effect of atipamezole on glucose- and Pi changes in autumn. This theory does not, however, agree with observations of *Ranheim et al.* (1997), who found no seasonal differences in the pharmacokinetics of medetomidine or atipamezole.

From the practical point of view, medetomidine alone seems to be a suitable sedation agent for reindeer, as also reported previously (*Tyler et al.* 1990 , *Ranheim et al.* 1997): rather fast and calm induction, good sedation, no drastic changes in blood chemistry, and calm, spontaneous recovery in a standing position within 8 h. In practice, a reversal with atipamezole is recommended to avoid possible complications and is even necessary in cold environments and in herds of reindeer. Resedation, which was observed within a couple of hours after atipamezole injection, has previously been described in forest reindeer (*Rangifer tarandus fennicus; Jalanka* 1989) and in reindeer (*Ranheim et al.* 1997) when atipamezole was given intravenously. In the latter study, resedation occurred 0.5 - 1 h after receiving atipemazole. This was explained by the longer elimination half-life of medetomidine than of atipamezole, which is contrary to the situation in, for instance, the dog, when atipamezole was given im (*Salonen et al.* 1995). Atipamezole also increased the medetomidine concentration in reindeer plasma (*Ranheim et al.* 1997). To avoid this undesirable phenomenon, different routes of administration of atipamezole could be used (i. m. or s. c.) and/or doses of it could be increased. More research is needed to find optimal dosing and routes of administration of reversal drugs to reindeer.

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Sammanfattning

Effekten av immobilisation med medetomidin och upphävning med atipamezol på blodkemin hos halvtama renar (Rangifer tarandus tarandus L.) under hösten och vårvintern.

Blodkemin undersöktes hos 8 vuxna honrenar, av vilka 5 var dräktiga. Den ena hälften av renarna fick endast medetomidin (150 μg/kg i.m.) medan den andra hälften fick både medetomidin och atipamezol (750 :μg/kg). Undersökningen gjordes i Mars.

Tre veckor senare upprepades provet men fördelningen av medicineringen var omvänd. Samma procedur upprepades också därpå följande höst i september och oktober.

Olikheter i blodvärden beroende av årstid kunde ses i följande blodvärden som var tagna före själva undersökningen. Koncentrationen av urea, fosfor och kolesterol var högre på hösten, medan kreatinin, ASAT, ALAT, och CK värden var högre på vårvintern hos icke dräktiga renar. Den protein- och energifattiga dieten under vintern antas vara den största orsaken till olikheterna i ovannämda blodvärden. Förhöjd enzymaktivitet i serum tyder på att vissa organs membran under vårvinter blivit mindre stabila, vilket möjligen är beroende av näringsbrist. Behandlingseffekten kunde ses i flera av dessa värden.

Förhöjningen av blodglukosnivåer och minskningen av fria fettsyror (FFA) var möjligen beroende av α2-adrenoreceptorernas aktivitet, vilka inhiberar utsöndringen av insulin och lipolysen.

Dessa effekter inhiberades helt eller delvis av antagonisten, atipamezol. Den snabbare förhöjningen av CK och ASAT aktivitet i serum kan dels förklaras med att atipamezol ökar vävnadsperfusion och dels att de djur som behandlats med konkurrerande preparat steg upp tidigare och rörde på sig mer än de djur som fick endast medetomidin. Den betydelsefulla minskningen av serum Na^+, K^+, Cl^-,

Pi, kolesterol, total Ca och total protein koncentration under de första 10 till 40 minuterna av nedsövningen med medetomidin kan möjligen förklaras med hemodilution och diures. Medetomidinets effektivare metabolism på hösten kunde förklara den kortare återhämtningstiden hos de av renarna som endast fick medetomidin, men också de flesta av olikheterna i behandlingseffekterna mellan årstiderna: snabbare ökning av protein- och kolesterolkoncentrationen efter minskningen och de antagonistiska effekterna av atipamezol på glukos och Pi värden. På basen av dessa resultat verkar det som att medetomidin har en bra sedativ effekt på renar under hösten och vårvintern; effekten av medetomidin kan ganska effektivt upphävas med hjälp av atipamezol.

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